

## REMARKS

Reconsideration is respectfully requested in view of the amendments above and the remarks below. Claims 1, 76, 85, 86, 88, and 90-95 have been amended. The support for the amendments is found at least in the originally filed claims 6 and 7, as well as in paragraph 335 of the instant application. Claim 76 is amended to correct an awkward linguistic structure which has been objected to. Claims 93 and 94 have also been objected to, and are amended to remove quotation marks. Accordingly, this Response does not add any new matter to the instant application.

The instant invention is drawn in general to synthetic Polyketide Synthase (PKS) genes or segments thereof, which retain significant similarity (95% or more) to the naturally occurring PKS genes or segments thereof at the amino acid level and which differ significantly (by 10% or more) at the nucleotide level.

More particularly, the instant invention is drawn, in one aspect, to a synthetic gene encoding a polypeptide segment, wherein said polypeptide segment corresponds to a reference polypeptide segment encoded by a naturally occurring polyketide synthase (PKS) gene, and a) the polypeptide segment encoded in the synthetic gene and the polypeptide segment encoded by the naturally occurring gene are the same length and comprise at least 50 amino acids; b) the polypeptide segment encoded in the synthetic gene and the polypeptide segment encoded by the naturally occurring gene are at least 95% identical in amino acid sequence; c) the polypeptide segment-encoding sequence of the synthetic gene and the polypeptide segment encoded by the naturally occurring gene are less than 90% identical in nucleotide sequence; d) the polypeptide segment encoded in the synthetic gene retains the activity of the polypeptide segment encoded by the naturally occurring gene; and at least one of: e) the polypeptide segment-encoding sequence of the synthetic gene is free from at least one Type IIS enzyme restriction site present in the polypeptide segment-encoding sequence of said naturally occurring gene; or f) the polypeptide segment-encoding sequence of the synthetic gene is different from the polypeptide segment-encoding sequence of said naturally occurring PKS gene and comprises at least two of: i) a Spe I site near the sequence encoding the amino-terminus of the module; ii) a Mfe I site near the sequence encoding the amino-terminus of a KS domain; iii) a Kpn I site near the sequence encoding the carboxy-terminus of a KS domain; iv) a Msc I site near the sequence encoding the amino-terminus of an AT domain; v) a Pst I site near the sequence encoding the carboxy-

terminus of an AT domain; vi) a BsrB I site near the sequence encoding the amino-terminus of an ER domain; vii) an Age I site near the sequence encoding the amino-terminus of a KR domain; viii) an Xba I site near the sequence encoding the amino-terminus of an ACP domain.

### Objections to Specification

The Examiner objected to the specification for the failure to recite the sequences which have been disclosed by their respective Genbank Accession numbers. Insofar as the Examiner is asserting that addition of a substantial amount of material is required, Applicants suggest this objection be addressed when the claims are otherwise indicated to be allowable.

Should the Examiner not be inclined to defer addressing this issue Applicants respectfully traverse. The Examiner has not indicated why it believes the information is essential.

Applicants respectfully draw the Examiner's attention to *Falkner v. Inglis*, 79 USPQ2d 1001, 1007 (Fed. Cir. 2006) indicating "there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of **known** structure" (emphasis added)

Indeed, the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification. Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences . . . satisfaction of the written description requirement does not require either the recitation or incorporation by reference

Also see *Capon v. Eshhar* 76 USPQ2d 1078 (Fed. Cir. 2005) indicating the BPAI "erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes" where the genes were novel combinations of known DNA segments. Also see MPEP § 2163 and MPEP § 2164.05 which states that "[t]he specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public." It is undisputed that the sequences designated by the recited accession numbers are "well-known to those skilled and already available to the public." Accordingly, Applicants believe that the requirement imposed by the Examiner is contrary to the case law and MPEP.

Nevertheless, solely for the purpose of expediting prosecution of the instant application, Applicants provide sequences for the structures recited in claim 92, and the specification is

amended to that extent. A Declaration to the effect that “the amendatory material consists of the same material incorporated by reference in the referencing application” as specified on page 3 of the Office Action is submitted herewith. Further, the replacement Sequence Listing section is submitted herewith.

The Examiner has also objected to the specification for inclusion of the hyperlink in paragraph 0310. Currently amended specification does not include this hyperlink.

Accordingly, for the reasons above, Applicants respectfully request the Examiner to withdraw the objections to specification.

#### **Objection to claims 76 and 92-94**

The Examiner objected to claim 76 due to the recitation “the each DNA.” Applicants amended the objected recitation to read “wherein each of the DNAs.” Applicants believe this amendment overcomes the objection.

The Examiner also objected to claim 92 because the organisms were not italicized. Applicants respectfully disagree with the Examiner’s interpretation of claim 92. The names recited in the claim are the names of compounds (e.g., erythromycin) rather than the names of organisms (e.g., *Saccharopolyspora erythraea*). Accordingly, Applicants respectfully submit that the Examiner’s objection to claim 92 should be withdrawn.

The Examiner objected to claims 93 and 94 for the use of quotation marks. Currently amended claims 93 and 94 do not include any quotation marks.

For these reasons, Applicants respectfully request the Examiner to withdraw these objection grounds.

#### **Rejection under 35 USC § 112, first paragraph (written description)**

The Examiner rejected claims 1, 3-15 and 69-95 as allegedly non-compliant with the written description requirement. Applicants respectfully disagree.

As an initial matter, Applicants note that in the interview on October 12, 2007 with Examiner Robinson and Supervisory Examiner Weber, it was indicated during the interview that claims essentially identical to claims 91-95 were in compliance with the written description requirement. See the Interview Summary prepared by Examiner Robinson and mailed October 17, 2007 which states in part “Agreement with respect to the claims . . . was reached” and

"Supervisory Examiner Weber informed Mr. Apple that the proposed claim language would not raise an issue under 35 U.S.C. 112, first paragraph written description or enablement and that the claims would be entered in an after final amendment." Applicants respectfully submit that the comments by the Examiner do not address the arguments set forth by the Applicants. Applicants also note the Examiner does not discuss claims 93-94, which are product by process claims.

Applicants further bring the Examiner's attention to MPEP § 2163 which states that

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116."

Emphasis added. Thus, Applicants note that the requirement is for a reasonable conclusion, not for a conclusion beyond reasonable doubt.

Essentially, the Examiner advances two arguments. First, the Examiner argues that the representative number of naturally occurring genes is disclosed. Second, the Examiner argues that the representative number of species within the invented genus is disclosed.

With regard to the disclosure of representative number of naturally occurring genes, the Examiner appears to believe the written description requirement requires that the specification provide examples of an unspecified ("representative") additional number of naturally occurring polypeptides or genes. This is not a requirement of § 112. Applicants respectfully remind the Examiner that MPEP § 2164.05 states that "[t]he specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public." Applicants further submit that the meaning of the term "the polypeptide segment encoded by the naturally occurring gene", i.e., the reference segment, would be clear to a person of the ordinary skill in the art. To further clarify the meaning of this term, Applicants state that this term encompasses all naturally occurring PKS genes.

Applicants further note that even if some research and/or mental steps are required to determine what has been invented, this fact does not mean that the claim is non-compliant with the written description requirement. See, e.g., MPEP 2163, which states that

For example, the presence of a restriction enzyme map of a gene may be relevant to a statement that the gene has been isolated. One skilled in the art may be able to determine whether

the gene disclosed is the same as or different from a gene isolated by another by comparing the restriction enzyme maps.

Applicants respectfully submit that it is within ordinary skill in the art to access the amino acid and nucleotide sequences of naturally occurring PKS genes, which are available in multiple databases (e.g., Swissprot, Genbank, and BLAST) and to identify the naturally occurring PKS genes and segments thereof, which are the closest to the segments at issue. Additional publicly available software tools allow routine comparison of these reference PKS segments with the PKS segments at issue. Accordingly, the Examiner's position is contrary to MPEP.

The Examiner's position is also contrary to the current case law. For example, in *Falkner v. Inglis*, the Court of Appeals for the Federal Circuit stated that

a requirement that patentees recite known DNA structures, if one existed, would serve no goal of the written description requirement. It would neither enforce the quid pro quo between the patentee and the public by forcing the disclosure of new information, nor would it be necessary to demonstrate to a person of ordinary skill in the art that the patentee was in possession of the claimed invention.

79 USPQ2d 1001; 448 F3d 1357 (Fed Cir 2006). The *Falkner* Court continued as follows:

Indeed, the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification. Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences . . . satisfaction of the written description requirement does not require either the recitation or incorporation by reference.

In *Falkner* an interference count was directed to vaccines comprising a poxvirus vector having a deleted or inactivated essential gene. Appellants argued that the Patentees had not described and enabled vaccines comprising a poxvirus vector having a deleted or inactivated essential gene because the patent did not identify *any* essential poxvirus genes or the inactivation of any such genes. In response, the Court held neither examples nor actual reduction to practice nor recitation of known structures nor incorporation by reference of literature describing known structures was required to comply with Section 112.

In another case, *Capon v. Eshhar*, 76 USPQ2d 1078 (Fed. Cir. 2005), the Federal Circuit faced a similar issue and similarly ruled that written description does not require recitation of known sequences. In *Capon* claims were directed to chimeric DNA encoding single-chain chimeric proteins for expression on the surface of cells of the immune system. The chimeric DNA combined a first segment encoding all or a portion of a protein "expressed on the surface of cells of the immune system" (e.g., a lymphocyte signaling protein) and a second segment encoding the single-chain variable ("scFv") domain of "a specific antibody" (e.g., unspecified antibodies against "tumor cells," "virus infected cells," and the like). The Board of Patent Appeals and Interferences held that neither party described "by reference to contemporary and/or prior knowledge in the art of the structure, formula, chemical name, or physical properties of many protein domains, and/or DNA sequences which encode many protein domains" and that neither application in interference was in compliance with the written description requirement.

The *Capon* Court vacated the decision of the Board and held:

The "written description" requirement must be applied in the context of the particular invention and the state of the knowledge. The Board's rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization. When the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh. Both parties state that a person experienced in the field of this invention would know that these known DNA segments would retain their DNA sequences when linked by known methods. Both parties explain that their invention is not in discovering which DNA segments are related to the immune response, for that is in the prior art, but in the novel combination of the DNA segments to achieve a novel result.

As in *Capon*, the present invention is not the discovery of naturally occurring genes, and recitation of specific gene sequences in the claims is neither necessary nor appropriate. Accessible literature sources, including GenBank, clearly provided, as of the relevant date, genes and their nucleotide sequences. Moreover, several exemplary large genes were described in detail. Applicants respectfully submit that any individual skilled in the art would recognize that Applicants had possession of the claimed invention.

With regard to the alleged lack of the representative number of species within the invented genus, Applicants respectfully note that they disclosed a new method for making

synthetic genes and has described novel synthetic genes made by this process. Using this method very large synthetic genes (e.g., > 20 kb) can be synthesized very rapidly, economically and accurately. A unique, identifying feature of the synthetic genes is that they can encode the amino acid sequence identical to that of a naturally occurring protein (e.g., a polyketide synthase) but have a nucleotide sequence that differs dramatically from the naturally occurring gene (e.g., a polyketide synthase gene). The synthetic methods disclosed by the instant inventors may be used to engineer very large synthetic genes with a variety of useful properties without undesirably changing the encoded protein.

The present specification teaches that the sequences of naturally occurring genes are known (for example, referencing GenBank, *see* paragraphs [0178] and [0352]). For illustration the specification provides numerous accession numbers from which one of skill can readily find protein sequences and corresponding gene sequences. Moreover, the specification provides a detailed description of several synthetic genes made according to the invention (see, e.g., Examples 7 and 9 and Tables 14A-B and 17A). These synthetic genes encoding nine large polypeptides (ranging from about 1,410 amino acids to >7,000 amino acids in length) with > 99.7 % sequence identity with the corresponding naturally occurring polypeptide but only 74-76% sequence identity with the naturally occurring gene.

Applicants respectfully re-iterate that the specification discloses over 85 kb of sequence listing disclosing synthetic PKS genes and respectfully request the Examiner to point out an MPEP requirement to disclose all species of a claimed genus. On the other hand, Applicants respectfully note that MPEP § 2163 explicitly states that “just because reduction to practice is sufficient evidence of completion, it does not follow that proof of reduction to practice is necessary in every case.” The Examiner is respectfully asked to explain what purpose would be served by provision of an additional 85, or 100, or 1000 kilobases of synthetic genes.

All currently amended independent claims recite a limitation that the polypeptide segment encoded in the synthetic gene retains the activity of the polypeptide segment encoded by the naturally occurring gene. This is not merely a functional limitation. The PKS modules have been relatively well studied and the conserved amino acids have been identified, either in the prior art or by the Applicants. See, e.g., paragraphs 0335-0351, disclosing analysis of multiple modules.

Accordingly, in this case, structure-function correlation is either known or can be easily accessed requiring no more than ordinary skill in the art. For example, comparative analysis of different PKS modules would reveal non-conserved amino acids. Mutations in these amino acids is unlikely to change the activity of the activity of the polypeptide encoded by the synthetic gene. In addition, it has been known in the art that conservative substitutions, such as, for example V->I, L->I, or M->I, as mentioned in paragraph 0341, are also unlikely to impair the activity of the polypeptide encoded by the synthetic gene segment.

Thus, Applicants respectfully note that structure-function correlation is present in the instant application because it is known in the art and/or because such analysis is within the expertise of a person of ordinary skill in the art.

Applicants submit that it would be clear to one of skill in the art, with undergraduate knowledge of the genetic code and the relationship between DNA and amino acid sequences, and guided by the teachings of the specification providing detailed description of the design of synthetic genes that the inventors had possession of the invention claimed. This position is supported by MPEP. See, e.g., MPEP 2163, which recites that

Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, but not necessarily any particular species.

In this case, Applicants claim a genus of the polynucleotide sequences rather than a specific sequence. Further, codon preference has been well known in the art. See, e.g., Kim et al (cited by the Examiner). See also paragraphs 0115-0116 of the instant application as filed.

In view of the above, Applicants respectfully submit that the claims of the instant application comply with the written description requirement and respectfully request the Examiner to withdraw the instant ground for rejection.

#### **Rejection under 35 USC § 112, second paragraph (indefiniteness)**

Examiner rejected claims 1, 3-15 and 69-95 as allegedly non-compliant with the definiteness requirement because the Examiner asserts that it is unclear how to distinguish a stretch of sequence that is synthetic from the naturally occurring one. See Office Action at 7. Applicants respectfully disagree and note that the segment of the synthetic gene, as recited in the claims, should be viewed as a whole (the way it is claimed), and not be considered as a



combination of nucleotide fragments, some of which may be present in a naturally occurring PKS gene. The claims specifically recite that the nucleotide sequence of the claimed gene segment should differ by at least 10% from the polynucleotide sequence of the naturally occurring reference genes. Accordingly, if a difference exists between the nucleotide sequences of the PKS gene segment at issue and the reference (i.e., naturally occurring) PS gene segment, the gene segment at issue is synthetic. Accordingly, Applicants respectfully submit that the ways of distinguishing a synthetic and natural PKS genes is definite and clear.

The Examiner further rejected claims 1, 3-15 and 69-95 as allegedly indefinite because no reference polypeptide structure is provided in the claims. Applicants respectfully disagree that this ground is proper for rejection under § 112, second paragraph. The specification recites, *inter alia*, Accession Numbers for ORFs of different PKS genes. See Application as filed, at pages 95-99, and claim 92. These and other naturally occurring sequences are available in public databases. The polynucleotide sequences of the ORFs of these PKS genes serve as reference peptides. Further, the meaning of the term “the polypeptide segment encoded by the naturally occurring gene” has been discussed and clarified above.

Applicants respectfully submit that a person of ordinary skill in the art would understand the language of the claims and would be able to define metes and bounds of the claims by comparing the sequence of a PKS gene at issue with the sequence of the closest naturally occurring PKS gene. If: a) the nucleotide sequence of the PKS gene segment at issue encodes at least 50 amino acids and differs by more than 10% from the nucleotide sequence segment of the closest naturally occurring PKS gene segment, which encodes the same number of amino acids; and b) the amino acid sequence of the PKS gene segment at issue is more than 95% similar to the amino acid sequence of the closest naturally occurring PKS gene segment; then the PKC gene segment at issue is encompassed by the claims.

Applicants respectfully note that software databases (e.g., Swissprot, Genbank, and BLAST) provide ample resources for obtaining the nucleic and amino acid sequences to find the closest naturally occurring PKS gene segment and perform the analysis above. Therefore, Applicants respectfully note that claims 1, 3-15 and 69-95 are definite and respectfully request the Examiner to withdraw this ground for rejection.

The Examiner also rejected claim 7 because the recitation “near” is allegedly relative. Applicants respectfully note that, taken in the context of the specification, the term “near” has a

clear meaning for each restriction site, as explained at least in Table 7 and 336-344. In fact, Table 7 even shows the nucleotide positions for each restriction site, as well as the amino acid sequence near that restriction site. Accordingly, Applicants urge the Examiner to read the term “near” in view of the specification, as described above, and respectfully request the Examiner to withdraw this ground for rejection of claim 7, as well as the independent claims, incorporating the disputed term.

**Rejections under 35 USC § 102(b).**

The Examiner rejected claims 1, 3-4, 6, 8-15, 69-71, and 92 as allegedly anticipated by Khosla (US 6,066,721) and/or Katz (US 6,004,787). Applicants respectfully disagree.

In order to anticipate a claim, a single prior art reference must disclose all limitations of that claim. In the instant case, this requirement has not been fulfilled. For example, neither Katz nor Khosla indicate that their respective polynucleotide sequences differ from the nucleotide sequences of naturally occurring PS modules by more than 10%. If the Examiner asserts that this limitation is disclosed by inherency, Applicants respectfully remind the Examiner that inherency may not be established by possibilities or probabilities. Instead, the undisclosed feature must be always and necessarily present in the prior art reference. MPEP § 2112. If the Examiner indeed insists that the nucleotide acid sequences of Katz nor Khosla differ from the naturally occurring reference nucleotide sequences, it is her burden to explain the reasoning behind this argument. See MPEP § 2112 IV. (“EXAMINER MUST PROVIDE RATIONALE (sic) OR EVIDENCE TENDING TO SHOW INHERENCY.”) Accordingly, the rejection based on anticipation of claims 1, 3-4, 6, 8-15, 69-71, and 92 by Katz nor Khosla is improper.

Nevertheless, in the interest of expediting the prosecution of the instant application, claim 1 has been amended to include, in the alternatives, the limitations of claim 6 and 7. Applicants note that the Examiner has not rejected claim 7 as allegedly anticipated by Katz or Khosla. Accordingly, the embodiments of claim 1, which recite the requirements of claim 7 are not anticipated by these references.

Applicants further respectfully note that the Examiner misinterpreted the limitation of claim 6, which recites that the polypeptide segment-encoding sequence of the synthetic gene should be “free from at least one Type IIS enzyme restriction site present in the polypeptide segment-encoding sequence of said naturally occurring gene.” The subject matter of claim 6 deals with the presence or absence of restriction endonuclease recognition site in the synthetic

gene of the instant invention. The fact that Khosla or Katz do not mention Type IIs restriction enzymes does not inherently (i.e., always and necessarily, see MPEP § 2112) indicate that the changes in the respective synthetic genes of Khosla or Katz are modified in such a way as to destroy the restriction site for IIs enzyme which are present in wild-type PS genes. As discussed above, the burden is on the Examiner to provide scientific rationale establishing that the polynucleotide sequences of Khosla or Katz are indeed modified in such a way as to remove at least one Type IIS enzyme restriction site present in the polypeptide segment-encoding sequence of said naturally occurring gene.

Therefore, in view of the amendments to claim 1 and the remarks above, Applicants respectfully submit that Khosla or Katz do not anticipate claim 1. Claims 3, 4, 6, 8-15, 69-71 and 92 depend on claim 1, either directly or indirectly, therefore incorporating all limitations of claim 1. Since claim 1 is not anticipated by Khosla or Katz, the claims dependent from claim 1 are also not anticipated by these references. Accordingly, Applicants respectfully request the Examiner to withdraw the instant ground for rejection.

#### **Rejections under 35 USC § 103(a).**

The Examiner rejected claims 1, 3-15, 69-71, 74, 75, 77-82, and 85-95 as allegedly obvious in view of the combination of Katz and Kim (*Gene*, 199: 293-301, 1997). Applicants respectfully traverse.

As discussed above, the independent claims have been amended to include, in the alternatives, the limitations of claims 6 or 7. Katz does not disclose or suggest these additional limitations.

Specifically, it is on the record that Katz is silent regarding the removal of at least one Type IIS enzyme restriction site present in the polypeptide segment-encoding sequence of said naturally occurring gene (see Office Action at 10), and therefore, it cannot suggest this limitation.

The limitation from claim 7 introduced into the independent claims of the instant application requires analysis of two issues: first, whether the references cited in the Office Action suggest the recognition sites for the specific recited enzymes, and second, whether the references cited in the Office Action suggest these recognition sites at specific recited locations. Applicants respectfully submit that Katz is silent regarding both the presence of the specific

restriction sites and the presence of these recognition sites at specific locations, as recited in claim 7.

Kim does not cure the deficiencies of Katz. Kim deals with a completely different gene (erythropoietin) and only discloses that the gene having codon optimization for yeast system is expressed in yeast at higher levels than the gene having wild-type (i.e., human) codons. Kim addresses codon optimization for increased expression of the target protein and does not address the selection of codons for introduction of restriction endonuclease recognition sites. Applicants respectfully submit that codon optimization for increased expression would not necessarily yield the codons forming a restriction endonuclease recognition site. Accordingly, Kim does not cure the drawbacks of Katz.

Applicants further respectfully note that the general teaching for introduction of selected restriction sites at selected positions of the synthetic gene of the instant invention is taken from the instant specification. This shows that the Examiner used an impermissible hindsight in rejecting claim 7.

Even assuming, but without admitting, that the references cited by the Examiner disclose that the restriction enzyme recognition sites may be introduced into the synthetic gene, Applicants respectfully note that a broad disclosure does not necessarily makes obvious any embodiment encompassed by this disclosure. Specifically, the references do not disclose or suggest introducing restriction sites for only eight specific enzymes at eight specific locations within the claimed synthetic gene, as disclosed, e.g., in paragraphs 0336-0344 and Table 7 of the specification. In contrast, catalog of New England Biolabs, Inc. (Ipswich, MA) discloses over 240 restriction enzymes (see, e.g., [http://www.neb.com/nebecomm/tech\\_reference/restriction\\_enzymes/alpha\\_list\\_of\\_sequences.asp](http://www.neb.com/nebecomm/tech_reference/restriction_enzymes/alpha_list_of_sequences.asp)). Applicants respectfully submit that aside from the extensive description of their own work, at the time of the instant invention there was no any motivation to select the restrictions sites for the specific enzymes at selected locations, as recited in the instantly amended claims 1 and 93-95.

Accordingly, for at least these reasons, independent claims 1, 85, 86, 88, 90, 91, and 93-95 are not obvious in view of the combination of Kim and Katz. Since the independent claims are not obvious over the combination of Katz and Kim, the claims dependent from these

independent claims are also not obvious in view of these references. Therefore, Applicants respectfully request the Examiner to withdraw the instant ground for rejection.

**CONCLUSION**

In view of these amendments and remarks, Applicants believe that the claims of this application are in condition for allowance and an early notice to this effect is earnestly solicited. If the Examiner does not believe that such action can be taken at this time or if the Examiner feels that a telephone interview is necessary or desirable, Applicants welcome the Examiner to call the undersigned at 609-844-3021.

The USPTO is authorized to charge Deposit Account No. 50-1943 for any charges in connection with this matter.

Respectfully submitted,

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